

## Detection of proteins, viruses, bacteria using scanning probe microscopy

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The use of probe microscopy techniques for the detection of biological macromolecules is a relatively new direction. In the works [1, 2] we propose biosensor for viruses, bacteria and proteins detection. In particular, the sialic acids were used for detection of influenza A virus as the biospecific recognition reagents to bind to hemagglutinin of the virus. For bacterial cells detection, the antibodies against surface antigenic determinants of the cells are placed on the sensory layer surface. Detection of biological agents in the biosensor is carried out by registration of the amplitude, phase, frequency and the quality factor of the mechanical vibrations of the piezoceramic biochip.

The biosensor includes a flow cell with a piezoceramic biochip, a peristaltic pump, and a control unit. Data processing is carried out on a personal computer using original software. To maintain a given constant temperature in the flow cell, a thermistor is installed, which simultaneously serves both to measure temperature and to heat the fluid in the cell. The biochip is a miniature piezoceramic disc with sensor layers on opposite sides. When the influenza virus or microalbumin is attached to the biochip sensor surface, the resonant frequency of the biochip changes. As a result of the pathogens interaction with the receptor layer, the effective mass and rigidity of the biochip changes, which is recorded by the shift of the biochip resonant frequency. The biochip design was successfully patented (patent # 2636048 Biosensor device for the detection of biological micro- and nano-objects).

To test the biochip's performance, an experiment was conducted to test the activity of antibodies on microalbumin. When comparing the results of measurements of different concentrations of specific antibodies to albumin (50  $\mu\text{g/ml}$  and 5  $\mu\text{g/ml}$ ), it was found that when the concentration of antibodies immobilized on a piezoceramic disk decreases, the range of changes in the resonance frequency decreases, which confirms the results obtained by ELISA.

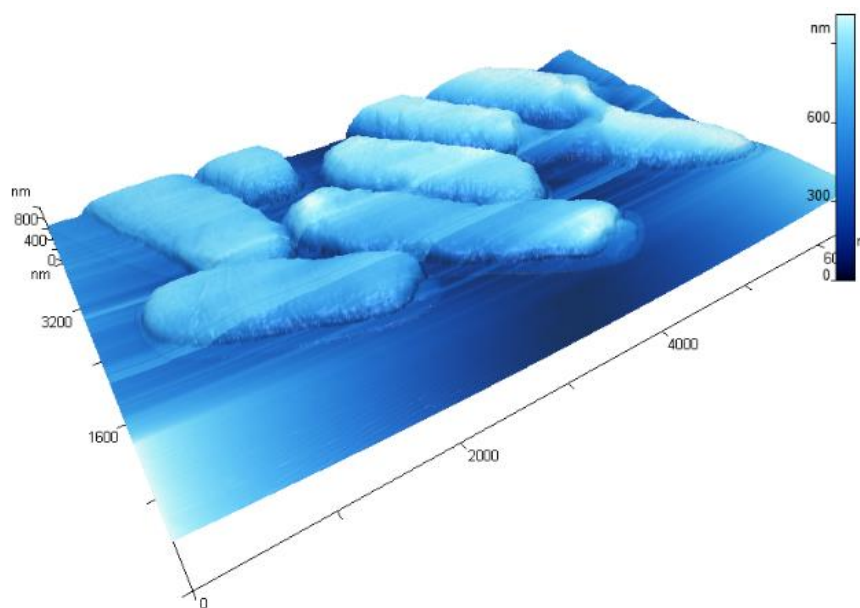


Figure 1. An image of the *E.coli* bacteria obtained using a FemtoScan scanning probe microscope and FemtoScan Online software.

1. A.I. Akhmetova, N. Gutnik, G. Meshkov, et al., *Nanoindustry* **70** (8), 22 (2016).
2. A.I. Akhmetova, I. Nazarov, G. Presnova, et al., *Nanoindustry* **49** (8), 44 (2017).